

### REMARKS

In order to expedite prosecution in this matter, applicants have amended the claims to more particularly point out the present invention. These amendments are editorial in nature and thus do not constitute new matter. Accordingly, their entry is respectfully requested.

Applicants appreciate the Examiner's acknowledgement that the specification is enabling for the *in vivo* methods taught herein.

Claims 1, 3-9 and 13-16 were rejected under 35 U.S.C. §112, second paragraph.

Specifically, the Examiner objected to claims 1, 6, 9, 13, 15 and 16. In order to expedite prosecution, applicants have amended claims 1, 9, 13, 15, and 16, and have used the language for suggested by the Examiner. As of our result of the amendment of claims 15 and 16, they now explicitly state that the nucleic acid is delivered into the cell.

Accordingly, applicants respectfully submit that the amendments to claims 1, 9, 13, 15, and 16 have obviated the rejection of these claims.

Applicants request withdrawal of the rejection of claim 6 for the reasons set forth below.

The Examiner contended applicant's discussion that the use of the species in that claim was not indefinite because the recitation of a protein family included its members was not persuasive because applicants had not pointed out where the specification made this clear.

The specification at pages 14 through 16 explicitly discuss the binding moiety and the particular sequences that can be used. See particularly the discussion at page 15. Applicants respectfully submit that from this discussion, particularly in view of the references cited therein, the skilled artisan would clearly recognize that the various molecules named in claim 6 all can constitute the binding moiety.

Accordingly, applicants respectfully submit that all claims comply with 35 U.S.C. §112, second paragraph.

Claims 1, 3-5 and 7-16 were rejected under 35 U.S.C. §103 as being unpatentable over Beug, et al. in view of Chaudhary, et al. and Wu.

Claim 6 was rejected under 35 U.S.C. §103 as unpatentable over Beug in view of Chaudhary and Wu as being applied above and further in view of Ryder, et al.

Applicants respectfully submit that these rejections should be withdrawn for the following reasons.

The law is clear that references must be read in their entirety, whereas picking and choosing isolated portions of a reference that do not reflect the teaching constitutes impermissible hindsight. Applicants respectfully submit this is what is happening here.

Applicants did not state that Beug **never** referred to the use of a fusion protein but rather that Beug was predominantly directed to using chemically synthesized conjugates. Indeed, that is what was exemplified. Similarly, applicants did not state that Wu **never** mentioned that an antibody could be used. In contrast, Beug **never** discussed using an antibody. The Examiner's citation to

Wu at Column 6 to demonstrate that Wu mentioned antibodies ignores the context in which the statement is made. The discussion actually began at column 5, lines 63 wherein Wu states:

As mentioned, this specific targeted delivery of genes to individual mammalian cells using a soluble carrier system is based on the fact that most if not all mammalian cells possess certain surface binding sites, referred to as receptors, that recognize and internalize specific ligands.

Thereafter, Wu taught:

Typically glycoproteins having certain exposed terminal carbohydrate groups are used although other ligands such as antibodies or polypeptide hormones, also may be employed. [Col. 6, line 3-7]

Wu's exemplification was the glycoprotein class, asialoglycoprotein. Beug never mentioned the use of an antibody using instead a glycoprotein, namely transferrin. Beug taught at page 3 that there are certain receptors that bind specific glycoproteins and convey them into the cell.

Thus the combined teaching of Wu and Beug is clearly and specifically directed to the use of glycoproteins that will bind to receptors. The reason is each individually teaches this point and their combined teaching merely reinforces the

importance of the receptors conveying the glycoproteins into the cell. The skilled artisan would not be taught by this combination to use an antibody, but specifically directed to a ligand glycoprotein that would bind a surface receptor and be brought into the cell. In contrast to such ligands, antibodies bind to specific epitopes. Even if an antibody that binds to a receptor was in some way a possibility, its effect would be unknown based on Wu and Beug teaching the importance of binding to receptors that will convey the glycoprotein into the cell and only exemplifying this. One would not know from these references that one could use an antibody because one would not know how whether the DNA carried along would be transported into the cell.

Accordingly, when these two references are read together they do not teach the skilled artisan to use antibodies because antibodies do not bind in the same way as the glycoproteins taught do. Indeed even when an antibody binds to receptor, it only binds to an epitope portion of that receptor.

Accordingly, the combination do not teach the desirability of using an antibody for the targeting moiety.

Similarly, even though in passing Beug mentions the use of a fusion protein, the exemplification in Beug is that of a chemical conjugate similar to the Wu. Accordingly, when these references are read together the skilled artisan would not be taught the advantage of a fusion protein. Again, the collective teaching points away from fusion proteins and to chemical conjugates.

The addition of Chaudhary to this combination adds nothing. While it talked about antibodies, it did not talk about their use in the system proposed.

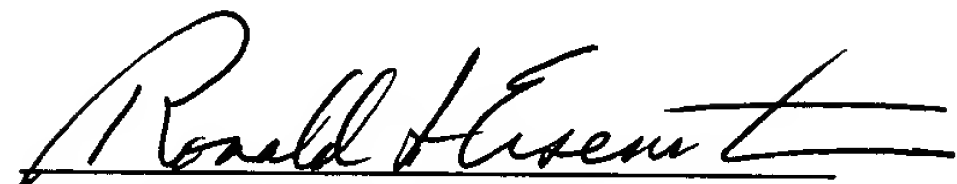
Similarly the addition of Ryder also does not overcome the deficiency because it adds nothing to the system.

Accordingly, applicants respectfully submit that this rejection of the claims should be withdrawn.

In view of the foregoing, applicants respectfully submit all claims are in condition for allowance. Even if the Examiner disagrees, applicants respectfully submit that this Amendment should be entered because it removes §112, second

paragraph problems and thus places the case in better condition for appeal. Early and favorable action is requested.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Ronald I. Eisenstein", with a horizontal line drawn underneath it.

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